SOLID STATE OLIGONUCLEOTIDE CONSTRUCTION USING ARYLOXYCARBONYL PROTECTION AND α-EFFECT NUCLEOPHILE DEPROTECTION

ABSTRACT

A method useful in a solid-phase oligonucleotide synthesis for removing a 5'- or 3'-protecting group from a protected nucleoside attached to a surface of a support, includes the step of reacting the protected nucleoside with a nucleophile that exhibits an α-effect at conditions of mildly basic pH. Also, a method for solid-phase oligonucleotide synthesis by sequential addition of protected phosphoramidites in which the protecting group is a carbonyl, includes following each phosphoramidite condensation by a treatment step under conditions of mildly basic pH employing a nucleophile that exhibits an α-effect. The treatment step removes the carbonyl protecting group and concomitantly oxidizes the internucleotide bond, so that separate deprotection and oxidizing steps are not required. Also, a kit for carrying out the oligonucleotide synthesis on a support includes a hydroxyl derivatized support surface, a protecting group for protecting the hydroxyl moieties on the derivatized surface, at least one protected nucleoside, at least one protected nucleoside phosphoramidite, a nucleophile that exhibits an α-effect at conditions of mildly basic pH, and reagents suitable for establishing the pH condition and for carrying out the reactions. Also, a method for creating an oligonucleotide array made up of array features presenting specified oligonucleotides at the various addresses on an array substrate includes steps of providing a protected hydroxyl derivatized array substrate surface, and then carrying out the two steps of (a) deprotecting selected feature addresses by exposing selected addresses to a droplet containing a nucleophile that exhibits an α-effect at conditions of mildly basic pH, and (b) flooding the substrate surface with a selected protected nucleoside phosphoramidite to couple the incoming phosphoramidite to the deprotected feature; and then repeating the two steps (a) and (b) to initiate and to extend oligonucleotides until the desired oligonucleotides have been constructed at the various features addresses.